Nucleosome dynamics *in silico* - Role of DNA and histone tails

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Nucleosomes form the fundamental building blocks of chromatin. Subtle modifications of the constituent histones tails mediate chromatin stability and regulate gene expression. For this reason, it is important to understand structural dynamics of nucleosome at atomic levels. We report a novel multi-scale model of the fundamental chromatin unit - nucleosome, having a simplified model for rapid discrete molecular dynamics (DMD) simulations and an all-atom model for detailed structural investigation. Using a simplified structural model, we perform equilibrium simulations of a single nucleosome at various temperatures. We further reconstruct all-atom nucleosome structures from simulation trajectories. We find that histone tails bind to nucleosomal DNA via strong salt-bridge interactions over a wide range of temperature, suggesting a mechanism of chromatin structural organization, whereby histone tails regulate inter- and intra-nucleosomal assemblies via binding with nucleosomal DNA. We identify specific regions of the histone core, termed cold sites, which retain a significant fraction of contacts with adjoining residues throughout the simulation, indicating their functional role in nucleosome organization. Cold sites are clustered around H3-H3', H2A-H4' and H4-H2A' inter-histone interfaces indicating necessity of these contacts for nucleosome stability. Essential dynamics analysis of simulation trajectories shows bending across the H3-H3' is a prominent mode of intra-nucleosomal dynamics. We postulate that effects of salts on mono-nucleosomes can be modeled in DMD by modulating histone-DNA interaction potentials. Local fluctuations in nucleosomal DNA vary significantly along the DNA sequence, suggesting that only a fraction of histone-DNA contacts make strong interactions dominating nucleosomal dynamics. Our findings suggest that histone tails have a direct functional role in stabilizing higher order chromatin structure, mediated by salt bridge interactions with adjacent DNA.